EXHIBIT B

IN THE UNITED STATES DISTRICT COURT
FOR THE SOUTHERN DISTRICT OF WEST VIRGINIA
CHARLESTON DIVISION

IN RE: ETHICON, INC., PELVIC REPAIR SYSTEM PRODUCTS LIABILITY LITIGATION	**Master File No. 2:12-MD-02327** **MDL 2327** **JOSEPH R. GOODWIN** **U.S. DISTRICT JUDGE**
THIS DOCUMENT RELATES TO: **Wave 4 Cases**	

TVT and TVT-O Expert Report of Elizabeth R. Mueller, MD, MSME, FACS

1. Background and Education:

I am board-certified by the American Boards of Obstetrics & Gynecology and Urology in Female Pelvic Medicine & Reconstructive Surgery and by the American Board of Urology in Urology. My current position is tenured Professor of Urology and Obstetrics/Gynecology, Division and Fellowship Director of Female Pelvic Medicine & Reconstructive Surgery (FPMRS) at Loyola University Chicago Stritch School of Medicine and Loyola University Health System. I am an internationally recognized leader in Female Pelvic Medicine & Reconstructive Surgery/Urogynecology for my expertise in the clinical and surgical care of women with urinary incontinence and pelvic organ prolapse as well as high-quality surgical outcomes and comparative effectiveness research. I received my medical degree from St Louis University School of Medicine in 1998 and was elected to Alpha Omega Alpha in the 3rd year of medical school.

Prior to my medical career, I was a practicing engineer for Procter and Gamble Manufacturing Company for 6 years. I ran a 100+ employee department and was responsible for the day-to-day manufacturing operation of high-speed packing lines and warehousing of Cascade dishwashing detergent. In addition I was a project manager of a technological change that was considered to be a potential biohazard and was responsible of $30 million technological change in the manufacturing process. I have a bachelor's degree in Mechanical Engineering (BSME) from the University of Missouri-Rolla, Rolla, MO in 1985 and a master's degree in Mechanical Engineering (MSME) with a certificate in Biomedical Engineering from Washington University in St. Louis, MO in 1988. My master's thesis involved the mathematical modeling of red blood cells and my thesis was titled "Extensional recovery of an intact erythrocyte from a tank-treading motion". I continued this work in red cell deformability when I went back to medical school.

I am a National Institutes of Health (NIH) funded investigator. I am currently a principal investigator involved in the Prevention of Lower Urinary Tract Symptoms (PLUS) consortium studying how to prevent lower urinary tract symptoms in women across the life span. I am a co-

investigator in translational research that is studying the urinary microbiome in women. I have over 75 peer-reviewed scientific research publications, many of which pertain to the etiology and treatment of urinary incontinence. I am involved in investigator initiated clinical trials looking at the impact of the anticholinergic medication on the urinary microbiome and sexual function in women. I was a co-investigator of a multicenter group who designed, implemented and published the largest US comparative effectiveness trial evaluating the TVT retropubic midurethral sling versus TVT-O and Monarc transobturator midurethral slings. The TOMUS RCT demonstrated the safety and efficacy of both TVT and TVT-O. Ethicon's TVTwas selected as the benchmark retropubic midurethral sling to be used in this study given the well-documented safety profile of the gold standard TVT mesh and procedure,

Listed below are the leadership positions that I have held in some of the largest professional organizations dedicated to improving the lives of women suffering from conditions such as stress urinary incontinence:

- Society of Women In Urology, President and served on the Executive Committee for 9 years.
- American Urogynecologic Society (AUGS) where I served on the Membership Committee (co-chair and chair), the Board of Directors, Program Committee Co-Chair and Chair, and Leadership Committee.
- American Urological Association where I served on the Executive Committee for the core Curriculum and the Committee for Overactive Bladder Practice Guidelines.
- Society of Urodynamics, Female Pelvic Medicine & Urogenital Reconstruction (SUFU) where I led the work group who developed a Urodynamics Curriculum for Urology Residents.
- American College of Surgeons, Fellow
- International Continence Society, Member

My Curriculum Vitae is attached as Exhibit 1 to this report.

2. Clinical Experience:

I completed my fellowship in 2005 and at that time in our fellowship when Burch colposuspension and bladder neck fascial slings were still considered first line surgical treatments of stress incontinence were Burch colposuspension and bladder neck fascial sling. I have performed over 200 Burch colposuspensions and 350 fascial slings. Both involve an abdominal incision and are significantly more invasive than midurethral slings. From 2002-2004,

I was a fellow when Loyola University Medical Center was part of a large federally supported comparative effectiveness trial comparing outcomes of Burch and bladder neck fascial slings, SISTEr (Stress Incontinence Surgical Treatment Efficacy Trial) directly comparing Burch and bladder neck fascial slings (Albo M. NEJM 2007). Unlike a case series evaluating autologous fascial slings, which is considered level 4 evidence, the SISTEr study provides level 1 evidence. We were taught by the attending phsycians (Linda Brubaker MD, MaryPat FitzGerald MD and Kimberly Kenton MD) how to perform the surgical procedures and they observed until we were felt to be competent to perform them under increasing levels of autonomy and eventually graduation.

In 2000, the National Institutes of Diabetes, Digestive and Kidney Diseases (NIDDK) established the Urinary Incontinence Treatment Network (UITN), recognizing the need for well-designed outcomes studies for urinary incontinence treatment in women as previous studies had methodological flaws and/or limitations that precluded definitive conclusions about the relative efficacy or differences in complications between procedures. These limitations included variability in case definition, failure to account for known confounders, lack of standardization of technique, short duration of follow-up, poor generalizability, inadequate power to detect clinically important differences, lack of assessment of complications, and marked variability in outcome assessment (UITN. Urology 2005). Randomized controlled trials or comparative effectiveness trials are considered the best of all research designs because the act of randomizing patients to receive one intervention or the other ensures that, on average, all other factors are equal between the groups. Therefore, any significant differences in outcomes or complications between the groups can be attributed to the intervention or procedure and not to some other factor. Burch and bladder neck slings were selected for comparison by the UITN since they were considered the ‘gold standard’ procedures for treating stress incontinence in the US at that time; although expert opinion existed regarding the efficacy of the procedures, no prospective comparative data was available to support or refute “expert opinions”. We now have 2-year and 5-year outcome and complication data directly comparing these two procedures (Albo M. NEJM 2007, Brubaker L. JAMA 2012).

The results from the landmark Ward Hilton RCT comparing TVT to Burch colposuspension

helped solidify TVT's position as a first line treatment option for SUI based on similar cure rates and quality of life with less morbidity ("postoperative complications were more common after colposuspension") and quicker duration of hospital stay, operative time, and return to normal activities. (Ward, Hilton BMJ 2002 & BJOG 2008). Subjective cure was similar between the two groups as well, as 85% of TVT patients were satisfied or very satisfied and 84% would recommend the procedure to a friend; compared to 82% and 82% for Burch colposuspension, respectively. Clinical studies continued to be published and the results all consistently demonstrated that TVT was revolutionary and a significant improvement from the traditional procedures. As part of practicing evidence-based medicine, I began introducing TVT to patients in the mid-2000s based on the increasing amount of clinical and scientific data available and the practice of the attendings who were my teachers (Linda Brubaker MD, MaryPat FitzGerald MD and Kimberly Kenton MD) and later my partners in our clinical practice.

Later, our team at Loyola University Medical Center began offering TVT-O as part of a NIDDK and UITN (Urinary Incontinence Treatment Network) clinical trial titled Trial of Mid-Urethral Slings (TOMUS). The trial was a federally funded comparative effectiveness trial of retropubic (TVT) and transobturator (TVT-O and Monarc) midurethral slings. The results of this trial helped to confirm synthetic midurethral slings as the first-line treatment option for SUI since they are less invasive, have fewer complications, less persistent voiding dysfunction, and lead to quicker recovery times for patients. Follow-up at 5 years confirmed the long-term efficacy and robust safety profile that is consistent with my the vast body of clinical literature evaluating TVT and TVT-O, as well as my clinical experience. (Richter HE. NEJM 2010, Albo M. J Urol. 2012, Kenton K. J Urol 2015).

As part of my clinical training, we were taught how to manage the complications that occur with incontinence procedures. In addition, we were taught how to counsel and advise women who could be identified as being at greater risk for complications. Women with multiple previous pelvic surgeries, radiation exposure, pre-existing pain conditions, symptoms of severe myofascial pain, neurological disease and preexisting pelvic floor conditions may present with stress incontinence as a late sign of their pelvic floor dysfunction. The symptoms of urinary incontinence can be complex and while women may believe they can be "fixed" by an

incontinence procedure, there are often many factors at play. Complications associated with incontinence procedures require experience and surgical judgment. This was emphasized throughout my training and my career. The complications associated with stress urinary incontinence procedures are commonly known. These elemental risks that can occur with any procedure, such as pain or dyspareunia, are taught in residencies and fellowships, widely published in the peer-reviewed medical literature and textbooks, discussed at conferences, and learned throughout training and clinical experience.

I have been offering synthetic midurethral slings, including Ethicon's TVT and TVT-O devices to patients since the mid 2000's, and continue to offer them today as a first-line treatment for SUI. I have significant clinical experience implanting both mechanically cut and laser cut midurethral slings without any clinically significant differences in safety (complication rates) or efficacy (durability and integrity of design properties). This is consistent with the highest level of clinical evidence in the peer review literature, including systematic reviews, meta-analyses, long-term studies, and hundreds of randomized controlled trials and clinical studies. The lack of any clinical significance between laser cut and mechanically cut TVT mesh is also consistent with my clinical experience in having performed over 950 TVT, both mechanically cut and laser cut and TVT Exact (laser cut) procedures, as well as over 150 TVT-O procedures.

As part of my armamentarium, I currently discuss the risks and benefits of the Burch colposuspension, autologous fascial sling, and synthetic midurethral sling procedures, although most of my patients choose the synthetic midurethral sling. For many of my patients, the potential benefit of a proven treatment option in the midurethral sling with high long-term cure rates and patient satisfaction, as well as less invasive, fewer complications, and quicker return to normal activity and voiding is significantly outweighed by the potential risk of mesh erosion or exposure, or other postoperative complications that can occur with any incontinence procedure. I do not offer biologic allograft slings as the clinical evidence is lacking. (Soergel 2001 Int Urogynecol J; Flynn 1999, J Urol; Fitzgerald 1999 BJU; Fitzgerald 1999 Am J Obstet Gynecol). Further, complications such as erosion and pelvic pain can still occur with allografts such as Repliform. (Bradley 2003, J Urol).

3. Materials Reviewed

My attached reliance list contains the materials that I have reviewed and relied upon in support of my opinions. A significant amount of the literature contained on my reliance list is literature that I have reviewed in the course of my career.

4. Expert Testimony:

I have given expert testimony in the following cases;

Illinois

- Whitcomb v. Horng
  McLean County Case #10L 119
  Testifying July 8, 2015

South Carolina

* Neighbors, et al v. Brown, MD, et al
C.A. File No. 11-CP-30-1137 On Appeal
Judgment: $1,115,464.33 (Pamela) $10,000 (Carroll)
Deposition and Trial Testimony

* Dennie, et al v. Brown, MD, et al
C.A. File No. 11-CP-30-1138 On Appeal
Judgment: $728,625 (Lisa) $880,820.19 (Jeffrey)
Deposition and Trial Testimony

* Mitchell (deceased) v. Brown, et al
C.A. File No. 11-CP-30-1139 Trial Scheduled August, 2015
Deposition Testimony

* Ward, et al v. Brown, et al
C.A. File No. 11-CP-30-1140 Trial Scheduled August 2015
Deposition Testimony

* McCord, et al v. Brown, MD, et al
C.A. File No. 11-CP-30-1141 Final Judgment
Judgment: $1,740,692.95 (Chris) $58,789.04 (Christopher)
Named Expert

* Sherfield, et al v. Brown, MD, et al
C.A. File No. 11-CP-1142 Final Judgment
Judgment: $1,468,800(Janice) $50,000 (Jerry)
Consulting Expert

5. Fees

I am charging $750 per hour for meetings and to review documents, $750 per hour for deposition testimony, and $8,000 per day for trial testimony. I have not testified as an expert in the past for Ethicon.

6. Medical Opinions:

My opinions are based on my education, training, professional experience, clinical research and teaching, my review of the medical and scientific literature, as well as my experience as a reviewer for the leading medical journals in my field. They are also a reflection of my annual participation in the annual scientific meetings that I have been attending since 2004, including the positions statements and systematic reviews and guidelines of these societies. All of my opinions are held to a reasonable degree of medical certainly. A summary of my opinions includes the following: (1) Synthetic Amid Type 1 macorporous polypropylene midurethral slings such as TVT and TVT-O are the gold standard, first-line treatment for SUI, and have essentially replaced the traditional procedures as a first line treatment; (2) Synthetic polypropylene midurethral slings have a favorable safety compared to alternative treatments and have been widely adopted and endorsed by the leading medical societies throughout the world and considered as the standard of care for treating SUI, which is in direct contrast to the opinions of a handful of plaintiffs' experts who do not represent the overwhelming majority of pelvic floor surgeons who consider midurethral slings to be the standard of care; (3) The TVT and TVT-O are reasonably safe for the surgical treatment of stress urinary incontinence, and no other procedure, design, biologic material or mesh has been demonstrated to be more effective, safer, or has been studied as much as, as long as, or in as many patients and types of patients as the TVT and TVT-O; (4) Gynecologists, urologists, and urogynecologists who treat stress urinary incontinence are expected to be knowledgeable in the success rates, complications, and management of complications associated with incontinence procedure, including synthetic midurethral slings, such as TVT and TVT-O; (5) The risks associated with midurethral slings are commonly known and well-described in the medical literature. Erosions can occur with any

material used in incontinence procedures; however, the erosion of synthetic mesh (as opposed to suture, autologous sling, or allograft) commonly described as the only unique risk of midurethral slings; (6) The IFUs, Monographs, and Professional Education materials for TVT and TVT-O adequately and accurately reflect the complications specific to the device that are described in the medical literature; and (7) There is insufficient reliable data supporting plaintiffs' experts' unsubstantiated theories that TVT causes complication due to alleged particle loss, degradation, cytotoxicity, roping, fraying, curling, carcinogenic potential, small pores, heavy weight, and mechanically or laser cutting of the mesh.

Prevalence of SUI:

Epidemiological data shows that over 35% of adult women in the US struggle with urinary incontinence. This leads to the general belief by most women that urinary incontinence is a "normal" function of aging. However, like hypertension, SUI is common but not normal. Urinary incontinence poses serious negative consequences to concentration, physical activity levels, self-confidence, and ability to complete work without requiring interruption, and for many women the symptoms are highly debilitating (Sinclair A, The psychosocial impact of urinary incontinence in women. The Obstetrician and Gynaecologist 2011). Women with severe and mild-moderate incontinence are 80% more likely to have depression compared to continent women in the same age group. (Nygaard I, Urinary Incontinence and depression in middle-aged United States women. Obstetrics and Gynecology January 2003). Despite the high prevalence and incidence, almost 90% of women with urinary incontinence never discuss their symptoms with their health care providers. Similarly, conditions such as overactive or underactive bladder and other bladder pain syndrome are rarely discussed with providers, leading to extended and unnecessary delays in diagnosis or treatment.

In the past, urinary incontinence has been considered a "quality of life issue" however; many thought leaders state that urinary incontinence has a direct impact on health. This is demonstrated in the following prospective cohort study of 180 patients 60 years or older with serious illnesses that were hospitalized at an academic center in Philadelphia (Rubin EB, States Worse Than Death Among Hospitalized Patients With Serious Illnesses. JAMA Intern Med. 2016;). Patients were asked to rate on a 5-point Lickert scale various health states. They were to

indicate whether they considered a "health state" to be worse than death, either better or worse than death, a little better than death, somewhat better than death or much better than death. The majority (68.9%) of patients in the study considered bowel and bladder incontinence to be equal or worse than death. Incontinence was the highest among the 10 states of disability which included "relying on a breathing machine to live", "confused all the time", "cannot get out of bed", "at home all day", "moderate pain all the time", "in a wheelchair", 'living in a nursing home", "relying on a feeding tube to live" and "need care all the time".

Treatment Options:

Non-surgical options for SUI included physical therapy, transvaginal incontinence devices and adaptive behaviors. The etiology of stress incontinence is a disruption to the neuromuscular (nerve and muscle) function of the pelvic floor. Nerve damage to branches of the pudendal nerve has been well documented in women undergoing childbirth. Not all of this damage is recoverable and while women may be able to compensate for the first 5-15 years after childbirth, in the normal process of aging the muscle mass of the pelvic floor starts to decrease. For some women, work with a physical therapist may restore some of the muscle compensation but cannot eradicate nerve damage or result in the growth of new nerves. The success rate of physical therapy varies but much like a person who has had nerve damage from a stroke, the success of physical therapy is highly dependent on the amount of recoverable nerve function, which is highly variable. Physiotherapy is associated with a broad variation in the rates of subjective (53-97%) and objective (5-49%) success, and more severe symptoms are associated with worse outcomes (Imamura M. et al, Systematic review and economic modeling of the effectiveness and cost-effectiveness of non-surgical treatments for women with stress urinary incontinence. Health Technol Assess 2010; Cammu H et al. Who will benefit from pelvic floor muscle training for stress urinary incontinence? Am J Obstet Gynecol 2004). After 3-15 years, 25-50% of women initially treated with physiotherapy have proceeded to surgery (Cammu H et al. Who will benefit from pelvic floor muscle training for stress urinary incontinence? Am J Obstet Gynecol2004;191:1152-7, Lamers HC, van der Vaart CH et al. Medium-term efficacy of pelvic floor muscle training for female urinary incontinence in daily practice. Int Urogynecol J Pelvic Floor Dysfunct 2007; Bo K, Lower urinary tract symptoms and pelvic floor muscle exercise adherence after 15 years. Obstet Gynecolo 2005).

In a 23 center, randomized trial, 460 women were randomized to physiotherapy or mid-urethral sling (retropubic or transobturator) surgery for their stress incontinence symptoms (Labrie J et al Surgery versus Physiotherapy for Stress Urinary Incontinence. N Engl J Med 2013). Women who were dissatisfied with the result of the assigned treatment were allowed to "cross-over" to the other approach. A total of 49% of women in the physiotherapy group and 11.2% of the women in the surgery group crossed over to the alternative treatment. Subjective cure rates were 85.2% in the surgery group and 53.4% in the physiotherapy group. The authors concluded "for women with stress urinary incontinence, initial midurethral-sling surgery, as compared with initial physiotherapy, results in higher subjective and objective cure at 1 year".

Pessaries are another conservative option for women with stress incontinence symptoms. They have to be removed for cleaning and for intercourse. Women who choose a pessary for treatment tend to be older, less sexually active and have less severe symptoms (Kapoor DS, Conservative versus surgical management of prolapse: what dictates patient choice? Int Urogynecol J Pelvic Floor Dystunct. 2009).

History of Surgical Treatments for SUI

The first surgical treatment for stress incontinence that became routinely used was the anterior colporrhaphy in the 1900's. The procedure is transvaginal and is not considered a treatment option in current practice for stress incontinence. At the same time (1910's) the retropubic sling made from gracilis (medial upper thigh muscle that was wrapped around the urethra) was also developed. Modifications of the procedure continued until the pubo-vaginal sling using the rectus fascia was developed in 1942. The procedure used today is a modification of the original procedure but still requires and abdominal incision and harvest of an autologous fascial graft. The 2009 American Urological Association's (AUA) Clinical Guidelines estimate the cured/dry rates of an autologous rectus sling to be 90% at 12 to 23 months and 82% at 48 months or longer. Cure rates are known to decrease with time. The robust long-term studies evaluating long-term cure rates with validated criteria is lacking with traditional incontinence procedures, especially

considering the dozens of long-term studies evaluating TVT over the almost 20-year lifespan of TVT.

Cadaveric slings use a cadaveric fascia instead of harvesting autologous fascia from the patient. The long-term durability of these procedures is questioned due to reports of graft failure and disintegration over time. Based on the 2009 AUA Clinical Guidelines, there are no longer-term efficacy studies (>48 months) of women with cadaveric graft retropubic slings and short-term cured/dry rates are 74% at 12 to 23 months. Biologic slings, including allografts, do not have proven long-term safety or efficacy, come with the potential risk of disease transmission, have limited availability, are expensive, and the quality of the cadaveric tissues is not going to be consistent as compared to a synthetic polypropylene sling.

The open cystourethropexy and colposuspension were used in the 1950's for stress urinary incontinence and continue in limited use today. Both of these procedures are considered open abdominal retropubic suspensions and elevate the bladder neck. The AUA Clinical Guideline's meta-analysis estimate for cured/dry rates at 12-23 months based on 1,085 patients is 82%. The cure rates at 24 to 47 months is 74-76% and > 48 month cured/dry rates are 73%. There is no similar data for laparoscopic retropubic suspensions and it is not considered a standard procedure for stress incontinence.

Injectable agents for stress incontinence are an option for patients who do not want to undergo more invasive procedures such as a sling or retropubic suspension. They are considered an inferior option to other surgical options such as slings and retropubic suspensions and have an efficacy of 48% at 12 to 23 months to 32% at 24 to 47 months.

Potential Complications of Incontinence Procedures:

Two large randomized trials comparing the open Burch colposuspension to tension-free vaginal tape and to the fascial sling were published in 2002 and 2007, respectively. These studies randomized 475 women to Burch colposuspension thus providing a solid basis for understanding complications that arise when a large number of surgeons are performing the procedure. Ward and Hilton (3) enrolled women from 14 urogynecology and urology centers in the United

Kingdom. Women were randomized to the open Burch colposuspension or the tension-free midurethral sling. Exclusion criteria included current need for, or previous history of, surgery for pelvic organ prolapse (POP). One hundred and forty six women underwent the Burch urethropexy. Women in the Ward-Hilton study had the following intra-operative and post-operative complications reported at 6 months: urinary tract infection (32%), de-novo detrusor overactivity on urodynamics (11%), wound infection (7%), voiding disorder (7%), bladder injury (2%), deep vein thrombosis (2%), and incisional hernia (2%). Although overall blood loss was higher for the colposuspension, there were no reports of vascular injury or retropubic hematoma in this series. The need for patient catheterization decreased over time, but remained substantial with 8% of women requiring catheterization after 6 months. There was no statistically significant difference in rates of catheterization and voiding dysfunction compared to TVT. In 2004, the authors reported the two-year follow-up data. Of the 146 women randomized to Burch urethropexy, 5 (3.4%) underwent surgery for stress incontinence, 7 (4.8%) surgery for POP and 5 (3.4%) had an incisional hernia repair. At two-years, 4 (2.7%) women continued to catheterize and 3 (2.1%) continued to have symptoms of UTI. On physical exam, the number of women with vault/cervical prolapse increased from 21% pre-operatively to 63% at 24 months, 18% of the women with POP were symptomatic. Over the same 2-year time period, vault/cervical prolapse rates increased from 16 to 29% in the TVT arm. In summary, when compared to TVT, Burch colposuspension at 24 months resulted in higher rates of enterocele, voiding dysfunction, and need for catheterization and a 4% lower rate of UTI.

In the Stress Incontinence Surgical Efficacy Trial (SISTEr) involving nine surgical centers in the United States, women were randomized to an open Burch colposuspension or autologous rectus fascial sling. A total of 329 women received a Burch colposuspension, however, 48% of the women had concomitant procedures for pelvic organ prolapse. The following adverse events were reported in women who underwent the Burch colposuspension: cystitis (50%), new onset urge incontinence (3%), incidental cystotomy (3%), surgical wound complications requiring surgery (2.4%), voiding dysfunction > 6 weeks (2%), recurrent cystitis leading to diagnostic cystoscopy (1.5%), bleeding (1%), ureteral injury (1%), incidental vaginotomy (0.5%), ureteral vaginal fistula (0.5%), erosion of suture into the bladder (0.5%), and pyelonephritis (0.5%). In summary, compared to a rectus fascial sling, a Burch colposuspension resulted in lower rates of

success for stress incontinence and lower rates of cystitis, urge incontinence, and voiding dysfunction. The long-term cure rates decreased from 42% to 13% cured in the Burch group compared to 52% down to 27% cured in the autologous fascial sling group. (Richter 2012). Other studies have reported on the late complications after Burch colposuspension, including but not limited to persistent dyspareunia, pelvic pain, suture erosions, incisional hernias, pelvic organ prolapse, recurrence, de novo urgency, recurrent UTIs, persistent voiding dysfunction. (Kinn 1995; Kjolhede 2005; Stanton 1985; Galloway 1985; Lose 1987; Demirci 2001; Wiskind 1992; Rardin 2007; Eriksen 1990; Christensen 1997; Albo 2007, and Mueller, Retropubic Bladder Neck Suspensions, Chapter 10, 2013).

With regard to injuries associated with the pubovaginal sling, 6.3% of pubovaginal slings are associated with urinary tract injuries (Summit, 1992). Erosion rates of up to 21% have been associated with traditional bladder neck slings that use synthetic materials (Beck 1998, Bent 1993, Bryans 1979, Muznai 1992). It is also a common complication of the Stamey needle suspensions of the bladder neck (Mundy 1993; Jarvis 1992). Studies compared autologous fascial slings to synthetic midurethral slings have demonstrated similar cure rates, but higher reoperations and complications, as well as lower improvements in quality of life after autologous slings. (Padmanabhan 2016; Trabuco 2009). Erosions of autologous slings and allograft slings have been described in the literature. (Golomb 2001; Bradley 2003).

A systematic review and metaanalysis from the Society of Gynecologic Surgeons (SGS) that included English language randomized controlled trials from 1990 – April 2013 was published in the American Journal of Obstetrics and Gynecology in July of 2014 (Schimpf 2013). In addition to reviewing objective and subjective outcomes, the SGS review group analyzed the adverse event information from 46 randomized trials and 39 non-randomized trials.

> *Dyspareunia* - The highest rates of dyspareunia were seen in the pubovaginal sling where the summary estimate was 0.99% (0.39-1.9%) in five studies with a total of 696 women enrolled. The rates were lower in retropubic TVT 0.0% (0.01-1.64%) in 2 studies with a total of 488 women enrolled and 0.16% (0.02-1.14%) in 6 studies with a total of 624 women enrolled.

Sling exposure - Sling exposure was also higher in pubovaginal slings of 5.4% (total enrolled 851) as compared to retropubic MUS at 1.4% (total enrolled 5684) and transobturator MUS at 2.2% (total enrolled 3253).

Return to operating room for sling exposure – the highest rates were in the obturator group (2.7%, study n = 518) followed by retropubic sling (1.9%, study n =1.9%), pubovaginal sling (1.6%, study n = 640) and Burch colposuspension (0.28%, study n = 0.28%, study n = 352).

Wound infections - Wound infections are also much higher in Pubovaginal slings (2.6%, n=174) and Burch colopsuspensions (7% n=269) compared to Retropubic slings (0.75%, n=5781) and Transobturator slings (0.74%, n=2348). This reflects the significantly smaller abdominal or thigh incision sizes of MUS (2 cm) versus 6-8 cm abdominal incisions of Pubovaginal slings and Burch colposuspensions.

Transfusions –Transfusions were highest in the Pubovaginal sling group at a rate of 1.9% (study n=515). Retropubic TVT rates were 0.4% (study n = 8105), Transobturator rates were 0.17% (study n=584). Burch rates were 0.0% (study n = 105).

Hematoma- Hematoma rates were highest in the pubovaginal group 2.2% (study n = 644) followed by Burch colposuspension 1.4% (study n = 542). Retropubic and obturator rates were lower, 0.88% and 0.59%, respectively (study n of 15,950 and 2,995, respectively).

Overactive bladder symptoms –were highest in the Pubovaginal sling (8.6%, study n = 558) followed by retropubic sling (6.9% study n = 3486), obturator sling (5.3% study n = 1485) and Burch colposuspension (4.3% study n = 387).

Retention rates lasting less than 6 weeks post-operatively - were highest with the Burch colposuspension (17%, study n = 288) followed by the pubovaginal sling (12%, study n = 1053) retropubic sling (3.1% study n = 7127) and obturator sling (2.3% study n = 2629).

Retention rates lasting greater than 6 weeks post-operatively - were highest with the Burch colposuspension (7.6%, study n = 288) followed by the pubovaginal sling (7.5%, study n = 1053) retropubic sling (2.7% study n = 7127) and obturator sling (2.4% study n = 2629).

Return to operating room for urinary retention – was highest in the pubovaginal sling (3% study n = 1667) followed by retropubic sling (1.2% study n = 3103), obturator (1.1% study n = 2342) and Burch colposuspension (0.0% study n = 522).

Groin pain- was highest with the Obturator sling (6.5% study n=1594) followed by Retropubic sling (1.5% study n = 1811), Burch colposuspension (1.1% study n = 364), Pubovaginal sling (0.34% study n =591).

Leg pain- was highest with the Obturator sling (16% study n=649) followed by Retropubic sling (0.62% study n = 322). There were no studies that reported leg apin for Burch colposuspension or Pubovaginal sling.

Bladder perforation – was highest in the Retropubic sling (3.6% study n = 11,390) followed by Burch colposuspension (2.8% study n = 753), pubovaginal sling (2.3% study n = 1069) and obturator (0.70% study n = 4,000).

Urethral perforation – was highest in the retropubic sling (0.41% study n = 2211) followed by obturator (0.20% study n = 1013) and Burch colposuspension (0.0% study n=25). Pubovaginal sling urethral perforation rates were not mentioned in any study but from personal experience can occur.

Deep vein thrombosis – was highest in Burch colposuspension (0.58% study n = 506) followed by Pubovaginal sling (0.35% study n =567) Retropubic sling (0.06% study n = 1660) and transobturator (0.0% study n = 68)

TVT Revolutionized the Treatment of Stress Urinary Incontinence:

Since its introduction in 1995 the midurethral sling (MUS) changed the paradigm for the treatment of stress urinary incontinence in women. TVT was developed by Ulf Umsten based on two hypothesis; 1) That a loose pubourethral ligament cause urinary stress incontinence, and that 2) A tape implanted in the exact position of a damaged pubourethral ligament would create a collagenous "neoligament" to reinforce it, restoring function and continence (Petros 2015). Dr. Ulmsten's early publications on TVT showed significant improvement in complication rates when he started using Ethicon's Prolene mesh as opposed to other synthetic materials, including GoreTex, Mersilene, and Marlex. Ethicon's Prolene TVT is an Amid type 1 macroporous, monofilament, light weight mesh with one of the largest pore sizes for midurethral slings, and unique biomechanical properties that have resulted in excellent clinical results that have been consistently reproduced in study after study. (Amid 1994; Amid 1997; AUGS, SUFU 2014 Position Statement; Dietz 2003; Deprest 2005; Boukerrou 2007; Moalli 2008). The mesh properties for several of the midurethral slings are shown below, with Ethicon's TVT pore size reported at 1,379 microns, or 1.3 mm (Moalli 2008).

Table 1 Textile properties (including load at failure) provided by the manufacturers listed at the top (AMS, American Medical Systems) describing the different meshes tested in this study

Mesh type	Gynecare	Boston Scientific	AMS	Bard	Caldera	Mentor
Mesh thickness	0.63 mm	0.66 mm	0.66 mm	0.62 mm	0.48 mm	0.27 mm
Pore size	1379 μm	1182 μm	1000 μm	1160 μm	698 μm	374 μm
Fiber size (diameter)	0.15 mm	0.15 mm	0.15 mm	0.13 mm	0.15 mm	0.08 mm
Weight (g/m^2)	100	100	110	81	140	70
Relative porosity	53.9%	57.7%	52.1%	N/A	68.2%	N/A
Load at failure	70 N	70 N	65.6 N	60 N	70 N	76 N
Mesh edges/features	Tanged	Tanged/heat sealed midsection	Tanged/tensioning suture	Tanged	Not tanged	Not tanged; sealed edges

The synthetic mid-urethral sling incorporated new thoughts about urinary incontinence and addressed three of the shortcomings of traditional anti-incontinence procedures. The first is that the MUS were not placed under tension. This thought was actually radical and results in the lower urinary retention and post-operative voiding issues (de novo urgency urinary incontinence). The second issue was the short operative and recovery times required due to the minimally invasive approach and the use of synthetic materials versus the use of autologous rectus fascia. The surgery can be completed under and hour and women can go home the same

day often without the need for an indwelling bladder catheter (often called Foley catheter). Lastly, it addressed the need for a procedure that could be performed by surgeons without advanced fellowship training.

Compared to standard procedures of autologous fascial sling and the Burch colposuspension, the synthetic MUS required less time (75 minutes less than the fascial sling and 15 minutes less than an open Burch), resulted in less de novo urgency or urgency incontinence (6% MUS vs. 17% fascial sling and 4% MUS vs 13% Burch colposuspension), required less hospital stay (0.5 days less for sling and 4 days less for open colposuspension) and was associated with a quicker return to normal activities (Ogah J, Minimally invasive synthetic suburethral sling operations for stress urinary incontinence in women. Cochran Database Systematic Review 2009). It is for these reasons that the MUS sling has received the recommendations of the following organizations.

The American College of Obstetricians and Gynecologists (ACOG) and the American Urogynecological Association (AUGS) co-authored a practice bulletin in November of 2015 with the intention of aiding practitioners in making decisions about appropriate obstetric and gynecologic care. In the practice bulletin, the authors state as Level A evidence the following…

> *"Synthetic mid-urethral slings demonstrate efficacy that is similar to traditional suburethral fascial slings, open colposuspension and laparoscopic colposuspension. Compared with suburethral fascial slings, fewer adverse events have been reported with synthetic mid-urethral slings. Voiding dysfunction is more common with open colposuspension than with synthetic mid-urethral slings."*

And as a Level A conclusion they also wrote that support the synthetic midurethral sling being a primary surgical treatment option:

> *"There are substantial safety and efficacy data that support the role of synthetic mesh midurethral slings as a primary surgical treatment option for stress incontinence in women."*

American Urogynecological Associate (AUGS) and the Society of Urodynamics, Female Pelvic Medicine and Urogenital Reconstruction SUFU) co-authored a position statement in 2014, which was re-released in 2016 with endorsements from the American Association of Gynecological Laparoscopists (AAGL), The American College of Obstetricians and Gynecologists (ACOG), National Association for Continence (NAFC), Society of Gynecologic Surgeons (SGS) and the Women's Health Foundation (WHF). The position statement found that the "polypropylene mesh midurethral sling is the recognized worldwide standard of care for the surgical treatment of stress urinary incontinence," and that it "is safe, effective, and has improved the quality of life for millions of women." The position statement highlights the following key points:

1. *Polypropylene material is safe and effective as a surgical implant. . . As a knitted implant for the surgical treatment of SUI, macroporous, monofilament, light weight polypropylene has demonstrated long term durability, safety, and efficacy up to 17 years.*
2. *The monofilament polypropylene mesh is the most studied anti-incontinence procedure in history . . . No other surgical treatment for SUI before or since has been subject to such extensive investigation.*
3.
4. *Polypropylene mesh midurethral slings are the standard of care for the surgical treatment of stress urinary incontinence and represent a great advance in the treatment of this condition for our patients. . . Full-length midurethral slings, both retropubic and transobturator, have been extensively studied, are safe and effective relative to other treatment options and remain the leading treatment option and current gold standard for stress incontinence surgery. Over 3 million MUS have been placed worldwide and a recent survey indicates that these procedures are used by > 99% of AUGS members.*
5.

The American Urological Association (AUA) stated the following in their 2011 and 2013 position statements:

Suburethral synthetic polypropylene mesh sling placement is the most common surgery currently performed for SUI. Extensive data exist to support the use of synthetic polypropylene mesh suburethral slings for the treatment of female SUI, with minimal morbidity compared with alternative surgeries. Advantages include shorter operative time/anesthetic need, reduced surgical pain, reduced hospitalization, and reduced voiding dysfunction. . .

Mesh-related complications can occur following polypropylene sling placement, but the rate of these complications is acceptably low. Furthermore, it is important to recognize that many sling-related complications are not unique to mesh surgeries and are known to occur with non-mesh sling procedures as well. . .

Multiple case series and randomized controlled trials attest to the efficacy of synthetic polypropylene mesh slings at 5-10 years. This efficacy is equivalent or superior to other surgical techniques. There is no significant increase in adverse events observed over this period of followup. Based on these data, the AUA guideline for the Surgical Management of Stress Incontinence concluded that synthetic slings are an appropriate treatment choice for women with stress incontinence with similar efficacy but less morbidity than conventional non-mesh sling techniques.

The AUA also reported on complications in the Appendix of its 2012 Guideline, noting complications for the following: **Pain:** Burch 6%, Autologous fascial slings 10%, Synthetic midurethral slings 1%; **Sexual Dysfunction:** Burch 3%, Autologous fascial slings 8%, Synthetic midurethral slings 0%; **Voiding Dysfunction:** Burch 10%, Autologous fascial slings (undetermined due to insufficient data), Synthetic midurethral slings 2%.

The International Urogynecology Association has also published a position statement on July 21st, 2014 with the concluding summary:

"There is robust evidence to support the use of MUS from over 2,000 publications making this the most extensively reviewed and evaluated procedure for female stress

incontinence now in use…the results of a recent large multi-center trial have confirmed excellent outcomes and a low rate of complications to be expected after treatment with MUS. Additionally, long-term effectiveness of up to 80% has been demonstrated in studies including one which has followed up with a small group of patients for 17 years

As a result, IUGA supports the use of monofilament polypropylene mid-urethral slings for the surgical treatment of female stress incontinence"

The Food and Drug Administration in 2013 (Considerations about Surgical mesh for SUI) performed a systematic review of the literature through 2011 and concluded that "The safety and effectiveness of multi-incision slings is well-established in clinical trials that followed patients for up to one-year," and that "The use of mesh slings in transvaginal SUI repair introduces a risk not present in traditional non-mesh surgery for SUI repair, which is mesh erosion, also known as extrusion."

Other professional societies and regulatory agencies have noted the proven safety record that has made synthetic midurethral slings the gold standard surgical treatment for SUI. (Royal Australian and New Zealand College of Obstericians (RANZCOG) 2014 Position Statement; National Institute for Health and Care Excellence (NICE) 2013; European Association of Urology (EAU) 2012; European Union Commission 2015 SCENIHR Report). Further, guidelines have suggested that materials other than polypropylene (such as PVDF) do not have sufficient clinical data to be recommended for urogynecologic use. (SCENIHR Report).

TVT is Reasonably Safe and Effective for the Treatment of SUI:

As discussed in the above sections comparing TVT to earlier procedures (pubovaginal sling and Burch colposuspension), TVT is reasonably safe and effective for its intended use of treating stress incontinence. In addition, long-term studies with more than 5 and 10 year follow-up have demonstrated the efficacy of TVT. (Aigmueller 2011, Cresswell 2008, Schiotz 2008, Liapis 2008, Jelovsek 2007, Song 2009, Prien-Lawson 2008, Celebi 2009, Holmgren 2005, Li 2011, Svenningsen 2013, Nilsson 2013, Serati 2012, Heinonen 2012, Olsson 2010, Song 2014, Reich

2011, Groutz 2011). Similarly, long-term studies support the safety and efficacy of TVT-O. (Liapis 2010, Angioli 2010, Groutz 2011, Cheng 2012, Serati 2013, Laurikainen 2014, Athanasiou 2014). These data are consistent with several level 1 meta-analyses and systematic reviews. (Ford 2015; Ogah 2011; Ogah 2009; Novara 2008; Cox 2013; Tommaselli 2015, Schimpf 2014). Lastly, professional organizations have consistently supported the use of the procedure as a first line surgical treatment for stress incontinence.

In addition, as eloquently stated in Charles Nager's expert opinion paper "Midurethral Slings: Evidence-Based Medicine vs. The Medicolegal System (Nager, 2016):

> *"Despite, the advertisements and litigation against midurethral slings most physicians continue to perform midurethral slings as their primary operation for stress incontinence. The reason is quite simple; most physicians are practicing evidence based medicine and the midurethral sling is the best procedure for their patients"*

Plantiffs' experts opinions regarding the safety, design and warnings of TVT lack reliable scientific support

Plaintiffs' experts' opinions that the TVT is defectively designed is not scientifically validated in Level 1 medical literature, which has consistently demonstrated that the TVT is safe and effective especially when compared to alternative surgeries. Although there is a substation amount of literature available, I have highlighted some of the level 1 systematic reviews and meta-analyses that are consistent with the position statements from the leading medical organizations ,and my clinical experience, in concluding that the TVT is reasonably safe and effective for the surgical treatment of SUI:

Ogah J (2009) Minimally invasive synthetic suburethral sling operations for stress urinary incontinence in women. The Cochrane Library (2009) evaluated 62 trials involving 7101 women were included. The Cochrane Review concluded that "synthetic suburethral sling operations are as effective as traditional suburethral slings, open retropubic colposuspension and laparoscopic colposuspension in the short term with less postoperative complications."

The Ford (2015) Cochrane Review on Mid-urethral sling operations for stress urinary incontinence in women evaluated 81 trials that included 12,113 women. This recent Cochrane Review concluded that, "Mid-urethral sling operations have been the most extensively researched surgical treatment for stress urinary incontinence in women and have a good safety profile. Irrespective of the routes traversed, they are highly effective in the short and medium term, and accruing evidence demonstrates their effectiveness in the long term. This review illustrates their positive impact on improving the quality of life in women with stress urinary incontinence." The Review also showed similarly low rates of mesh exposure of around 2% for both retropubic and transobturator slings. The rates of groin pain and suprapubic pain were similarly low and described as being short in duration. They reported no significant differences between inside-out and outside-in transobturator slings. Further, they noted that "The reported occurrence of problems with sexual intercourse including pain was low, and leakage of urine during intercourse are improved following insertion of these tapes."

Schimpf (2014) as part of the SGS review group conducted a systematic review of English language randomized trials from 1990 to 2013 with a minimum of 12 months of follow-up comparing a sling procedure for SUI to another sling or Burch procedure. There were 49 randomized trials reviewed and 39 non-randomized trials were added to review adverse events. The author's summary states, "This review supports the use of MUS for treatment of SUI compared to pubovaginal slings".

Kenton (2015) reported on 404 women who agreed to be followed for 5-years in an observation cohort that originally randomized 597 women to retropubic or transobturator sling TOMUS trial. Satisfaction decreased over 5 years but continued to remain high and similar between the two arms (retropubic 79% and transobturator 85%, p=0.15).

There is a lack of scientific data supporting the plaintiff experts' claim that TVT is defective because of degradation, roping, curling, fraying, particle loss, cytotoxicity and potential to cause cancer. For example, Thames (2016) demonstrated the fallacies of previous studies that have hypothesized about degradation. Recent studies have demonstrated that polypropylene midurethral slings are not carcinogenic. (Moalli 2014; King 2015; Adel 2016; Linder 2016).

Mesh exposures have been reported when lighter weight, larger pore meshes have been used for slings (Okulu 2013) and prolapse meshes (Denis 2004; Milani 2011). Further, a survey conducted by Ethicon showed that two-thirds of the surveyed surgeons saw no need to design a partially absorbable sling since what they had already worked well, and the other third was cautiously optimistic. Ethicon conducted testing on a lighter weight, larger pore, partially absorbable sling, but it failed multiple cadaver labs (Elbert 2012 Memo – Eth.Mesh.09922570), and the 510(k) clearance was denied by the FDA. The medical literature, Ethicon's internal complaint evaluation, and my constant analysis of my clinical outcome data has not demonstrated any significant different between TVT mechanically cut versus laser cut. While there may be internal documents reporting surgeon preference (both for mechanically cut and for laser cut), and some destructive testing at 50% elongation without the protective sheaths, there is no reliable clinical data demonstrating a clinically significant difference.

In conclusion, the benefits of TVT and TVT-O outweigh the risks. The potential risks of midurethral slings are similar to those of the traditional procedures and are commonly known. There is a risk of erosion with any foreign body or autologous graft, but that complication with TVT and TVT-O is acceptably low at around 2% on average. I feel fortunate to have helped the lives a many women suffering from incontinence with minimally invasive procedures such as TVT and TVT-O.

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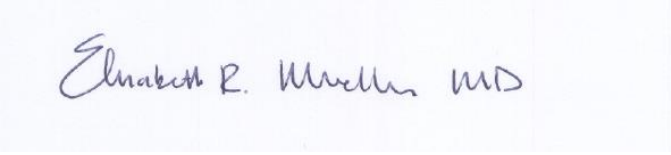

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